Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Title A Phase III Study to Assess the Effect of AZD0780 on Low Density Lipoprotien Cholesterol in Patients with Clinical Atherosclerotic Cardiovascular Disease or are at Risk for a First Atherosclerotic Cardiovascular Disease Event

Short Title	AZURE-LDL
Protocol Number	D7960C00012
Project Sponsor	AstraZeneca Pty Ltd
Principal Investigator	Dr. Andrew McCann
Study site	Life Clinical Research, 33 Thorn Street, Ipswich, QLD 4305

PART 1 What does my participation involve?

1 Introduction

You are invited to take part in a clinical research project. This is because you have elevated levels of LDL-C in your blood (hyperlipidaemia) and are currently receiving standard medical treatment for your hyperlipidaemia, and have Atherosclerotic Cardiovascular Disease (ASCVD) or are at risk of having an event of ASCVD. The research project is testing a new potential treatment for hyperlipidaemia (elevated LDL-C). The new treatment is called AZD0780.

This Participant Information Sheet and Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use and sharing of your personal and health information as described including the possible sharing of this information outside Australia.

You will be given a copy of this Participant Information Sheet and Consent Form to keep.

2 What is the purpose of this research?

We are doing this study to learn about the experimental drug AZD0780 and its safety, efficacy and tolerability in patients with elevated LDL-C and clinical ASCVD or who are at risk for a first ASCVD event, and also to better understand the studied condition and associated health problems.

AZD0780 is a newly developed oral tablet (medication) designed to treat Hyperlipidaemia, a disease characterized by high levels of lipids (fats) in the blood, including Low-density lipoprotein cholesterol (LDL-C). Several risk factors, such as, an unhealthy diet, lack of exercise, smoking, genetics and other underlying health issues, can increase the risk of developing hyperlipidaemia. Hyperlipidaemia is one of the main contributing factors to serious conditions like heart attacks and strokes. When cholesterol builds up in the walls of blood vessels, it can lead to a condition called atherosclerosis, where the arteries become narrow and hardened. This restricts blood flow to vital organs, increasing the risk of life-threatening conditions such as heart attacks, strokes, and other cardiovascular diseases. These conditions resulting from restricted blood flow are collectively called atherosclerotic cardiovascular disease (ASCVD).
A protein called PCSK9 has been identified as an important substance in the regulation of LDL-C levels. AZD0780 is a drug that inhibits the function of PCSK9 and thus is expected to accelerate the breaking down of LDL-C and reduce LDL-C levels in the body. Reduced LDL-C is expected to delay or prevent the occurrence of atherosclerotic cardiovascular events. We are doing this study to learn more about how AZD0780 affects LDL-C levels and levels of other types of fat in your blood and assess its safety and how well participants can handle the study treatment without significant discomfort or side effects.

Medications, drugs and devices must be approved for use by the Australian Federal Government's Therapeutic Goods Administration (TGA).

AZD0780 is not an approved treatment for ASCVD or any other condition in Australia, therefore it is an experimental treatment in this study.

Your data and test samples are needed for the Sponsor to develop the drug, get approval for use, monitor its safety and get it reimbursed by governments. This is known as the drug development program. They will be used as planned in this study as well as within related research activities in order to:

- Understand how the study drug(s) and similar drugs work in the body
- Better understand the studied disease and associated health problems,
- Learn from past studies to plan new studies or improve scientific analysis methods,
- Publish research results in scientific journals or use them for educational purposes

This research is being conducted by AstraZeneca AB and sponsored in Australia by AstraZeneca Pty Ltd.

3 What does participation in this research involve?

If you agree to take part in this study and the study is suitable for you, your participation will last approximately 56 weeks.

The study will have 3 periods:

1. **Screening Period** before you start taking the study treatment: up to 2 weeks and 1 study visit.
2. **Treatment Period** when you will be randomised to study drug or placebo: up to 52 weeks and 9 study visits.
3. **Follow-up Period** after you have finished taking the study treatment: up to 10 days and 1 study visits.

Screening Period:

Before any study-related procedures are done, the study doctor will explain the study to you, give you time to read this Participant Information Sheet and Consent Form and answer any questions

you may have. If you agree to participate in the study, you will need to sign and date this consent form. You will be given a copy of the signed Participant Information Sheet and Consent Form to keep and the original copy will be put in your medical record. Your study doctor will also inform your local doctor (your GP) that you are participating in this research study.

The purpose of the Screening Period is to make sure you are suitable to take part in this study. The Screening Period will take place over a 2 week period. During the Screening Period you will need to have some examinations, tests, or procedures. The information and samples collected will be kept and used with the rest of the study results.

These tests are sometimes part of regular medical care. They may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This is up to the study doctor.

You may go through the screening procedures a second time if you don't meet the screening criteria at the first visit.

If your study doctor finds that you qualify for the study, you will be enrolled into the study and start the Treatment Period. If the results of the screening tests show that you do not qualify for the study, you will not be able to participate. Your doctor will discuss your alternative treatment options with you.

All data collected with your name and contact details will be identified by a code. This is done by the study doctor who keeps the link between your name/ contact details and the code to ensure your safety and confidentiality. The study site will forward your data and test samples to the sponsor only after they have been coded therefore the data is not able to identify you.

Your study doctor will also ask whether you are willing to participate in 2 optional sub-studies:

1. **Optional Genomics Initiative Research**: participants can consent to provide blood samples for DNA and multi-omics analysis, which includes genomic and comprehensive omics characterisation research. This will be discussed with you in a separate consent form
2. **Optional Future Exploratory Biomarker analysis**: participants can consent to provide urine and blood (plasma) samples for future exploratory biomarker research. Please see further below for details regarding future research.

For the optional exploratory biomarker analysis, you can opt in or out on the consent page of this document. If you are potentially interested in the **Optional Genomics Initiative Research**, you will be given a **separate Participant Information Sheet and Consent Form** to consider. You can decide whether or not to take part in both of these optional sub-studies.

Treatment Period

If your study doctor confirms this study is suitable for you and you agree to continue in this study, you will be asked to return to the clinic to start your study treatment.

In this study, there will be 2 treatment groups. You have a 1 in 2 chance of being given AZD0780 or placebo.

The 2 treatment groups are:

1. AZD0780 - 30 mg
2. Placebo

From this point on in this document the term 'study drug/s' may be used to refer to both treatment groups.

You will be participating in a double-blinded study which means that neither you nor your study doctor will know which treatment you are receiving. This helps to make sure the researchers interpret the results properly and avoids study doctors or participants jumping to conclusions. However, in certain circumstances your study doctor can find out which treatment you are receiving.

There may be a break between treatments so that the first drugs are cleared from your body before you start the new treatment.

A placebo is a medication with no active ingredients or a procedure without any medical benefit. It looks like the real thing but is not.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.

You will only be given AZD0780 while the study is going on but not after it has ended.

The study treatment will be given to you as an oral tablet *taken once daily by mouth.* It should be taken with or without food.

During the Treatment Period, you will need to attend the site for at least 10 visits over 52 weeks. Each visit may be different in length depending on what tests will be done. Your study doctor will explain what you have to do, and which tests you will have during the study. Each visit will take between 1 and 3 hours. A full description of the required assessments is listed below and on the ***Table 1 - Schedule of Assessments***. You will need to fast 8 hours prior to coming for each visit. You are allowed to drink during this period of fasting.
To conduct the study, some tests and procedures will have to be performed to monitor your progress and ensure your safety. The section "Required tests and Procedures" below provides details. If you cannot come to a visit, you must tell your Study Doctor

Follow-up Period:

After you finish taking the study treatment for whatever reason, you will need to return to the study site for a follow-up visit at 10 days after Visit 10 (End of Treatment Visit).

The study staff will provide you with full details of your specific follow-up schedule. If you cannot come to a visit, you must tell your Study Doctor.

If your study treatment is stopped before the end of the study, you will attend the "Stop Early" visit as soon as possible after the treatment is stopped. Your study doctor will recommend that you continue on the study and follow the original visit schedule without taking study drugs. If you do not want to continue with all the study visits, a modified follow-up schedule can be arranged.

Required Tests and Procedures:

During the study visits, you will have required tests and procedures which are described below and listed in the table attached at the end of this Participant Information Sheet. Your study doctor will also explain what you will have to do and the tests that you will have during the study.

The following tests and procedures will be required as part of this study:

- **Medical History:** You will be asked to tell the study staff about past and present medical conditions, diseases, and surgeries. Your study staff will also request a record of your medical history from your GP and / or referring physician.

- **Demographics**: Information about your birth date, sex, race, and ethnicity will be collected. Details of race/ethnicity will be used for research purposes only to understand if people from different race/ethnic backgrounds respond differently to AZD0780.

- **Physical examination:** This will include checking your general health as well as how your disease is progressing. It will include checking your general appearance, lungs, circulatory system, stomach, skin, head, neck, thyroid, as well as your immune, muscular-skeletal, and neurological systems. Your height, weight and waist circumference will also be measured.

- **Medications Review/Side Effects:** The study team will discuss any medications that you may be taking. Please inform them about all the drugs you are taking, including prescriptions and those that you can buy without a prescription. You will also be asked if you have been feeling unwell or have noticed any changes in your health. You must tell the study staff about any changes that have occurred since your last visit.

- **Measurement of vital signs:** Vital sign measurements, including blood pressure, heart rate, breathing rate, blood oxygen levels and body temperature, will be assessed.

- **Blood tests:** At most visits throughout the study, blood samples will be taken. The amount of blood taken at each study visit will vary and could be up to 30 mL (approximately 1.5 tablespoons*).* A total of about 125 mL (approximately 7 tablespoons*)* will be taken during the study. As a comparison, 450-500 mL (approximately 22-25 tablespoons) of blood is taken at a typical blood donation in a single day.

  You will be required to fast (no food or drink except small sips of water) for 8 hours prior to attending all study visits where blood is being taken. You will be able to eat and drink after your blood tests. Your study doctor will explain that **the study drug should not be taken in the morning before study visits with blood sampling**. On the study visit days, the study drug should be taken after the blood sampling has occurred. You will also be asked to bring your study medication, even if the bottles are empty, to each study visit.

  Extra blood tests may be taken if your study doctor believes they are needed for your safety and health. Your blood will be tested for:

  - Haematology and chemistry: The samples will be taken to check if there is anything that prevents you from participating in the study, and then throughout the study to check your health including blood cell counts, liver and kidney tests, electrolytes and thyroid function.

Pregnancy test: If you are a woman who is able to have children, you will have a blood pregnancy test at screening and a urine pregnancy test at some other visits.

  - Exploratory biomarkers (Pharmacodynamics): A biomarker is a substance found in the body that is useful for measuring or predicting the progress of a condition or the effects of a treatment. This testing will measure proteins and other elements that might show how your disease responds to the study drug, to help learn more about hyperlipidaemia*,* and to assess how the study drug works.

- Study drug and Gene Interaction (Pharmacogenomics): To determine how genes affect the response of your body to the study drug. Blood and buccal (cheek) swab samples will be collected before giving the study drug.

- Hepatitis testing: Your blood will be tested at screening for Hepatitis B and C. Before the tests are done, you will receive information and counselling.

  If you test positive for one Hepatitis C test (Hepatitis C antibody), your doctor may be able to do another Hepatitis C test that tests levels of the virus load in your blood. If that test is negative, you may be eligible for the study.

  If a test shows you have Hepatitis, , or any other reportable diseases, you will have follow-up counselling and medical advice. If your test results are positive, the study doctors are required by law to notify government health authorities. Signing the consent form means that you agree to have this testing; it will not be done without your consent.

- **Urine Test:** Urine samples will be collected and tested to check your overall health. This testing will be done at screening and as needed throughout the study.

- **Pregnancy Test:** Women who are able to have children will have a pregnancy test (blood). You cannot take part in this study if you are pregnant. If you are a woman who can get pregnant, you will need to have a blood pregnancy test at screening and a urine pregnancy test at other visits.

- **Electrocardiogram (ECG):** This measures of the electrical activity of the heart. The ECG is done by placing small stick-on pads onto your skin and attaching sensors (electrodes) that can detect the electrical activity of your heart. It will be recorded after you have been lying down for 5 minutes.

Optional Tests and Procedures:

Plasma and Urine Samples for future biomarker analysis are optional in this study. If you agree, you may provide your consent by ticking the checkbox in the consent form. If you don't consent to the optional procedures, you can still participate in this study.

An extra sample for genomics and multi-omics analysis at randomisation may be collected during the study for optional tests.

You can still take part in this research study, even if you do not agree to donate the extra sample(s). If you decide to stop taking part in the study, please tell your Study Doctor if you want to change your mind about the use of your extra samples being used for analysis in this study.

The Table below lists the study tests and assessments. Additional tests, assessments and blood samples, may be collected at any time during the study if the study doctor considers it necessary.

Table 1 – Schedule of Assessments

Procedure	Screening Period	Treatment Period								End of Treatment/stop early visit	Follow-up Period
Visit (V)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**10 days after last dose**
Days (D)	**-14 to -7**	**0**	**14**	**28**	**56**	**84**	**112**	**196**	**280**	**364**	
Weeks (Wk)	**-2 to -1**	**Wk 0**	**Wk 2**	**Wk 4**	**Wk 8**	**Wk 12**	**Wk 16**	**Wk 28**	**Wk 40**	**Wk 52**	
Medical History	X										
Eligibility review	X	X									
Medications Review/Side Effects	<---------- X ---------->										
Demographics	X										
Physical Examination	X	X	X	X		X	X	X	X	X	X
Vital Signs	X	X	X	X		X	X	X	X	X	X
Height[1], Weight and waist	X	X						X		X	X
Blood Tests	X	X	X	X	X	X	X	X	X	X	X
Urine Tests	X	X	X			X		X		X	X
Pregnancy[2] blood and urine	X	X		X	X	X	X	X	X	X	X
ECG	X	X	X							X	X
Study drug dispensing and compliance check		X		X	X	X	X	X	X		
Study drug dosing		<---------- X (one tablet, once a day) ---------->									
Optional Biomarker samples[3]		X								X	

[1] Height taken at screening only
[2] For women of childbearing potential only
[3] Only if consent is given (end of this document)

What are the costs of taking part?

There are no additional costs associated with participation in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

If applicable, you may be reimbursed for reasonable expenses associated with your participation in the study (for example: parking). If so, you will be paid $80 at each study visit to cover your actual travel costs by direct deposit to your nominated bank account.

4 What do I have to do?

If you decide to take part in this study, there are some rules you must follow, some of which are listed below. There could be other rules that your study doctor will review with you.

You must follow your study doctor's instructions, take study drugs, and have all the tests and examinations described below. The tests and procedures are done for your safety and to check your health status.

- It is likely that you will have to come for clinic visits more often than you would if you were not in the study, but you must come to all scheduled visits requested by the study team.
- Report everything that is troubling your health to your study doctor.
- It is also important that you tell the study staff about any other medicines, vaccine, vitamins, or herbal supplements you are taking during the study.
- You should not take any medication restricted for this study including Lomitapide, Mipomersen, Gemfibrozil, PCSK9 Inhibitors or any Medications known to cause QT Prolongation
- You are not allowed to take part in any other research study with an experimental treatment while you are in this research study.
- If you have any health care contact such as with a different doctor or a dentist, you must tell them that you are in this research study.

Vaccinations: Please talk to your study doctor before you have any vaccinations, as live attenuated vaccines may not allowed from when you sign this consent form. A live attenuated vaccine is a form of the disease-causing agent (e.g. virus) which has been weakened so that it can create an immune response without causing disease.

5 Other relevant information about the research project

The research study is planned to go on for approximately 1 year and 10 months and includes around 2800 people with Atherosclerotic Cardiovascular disease or at high risk of first ASCVD event from about 22 countries including 60 in Australia.

6 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information Sheet and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Life Clinical Research.

Please take as much time as you need to make a decision about whether or not you would like to participate in this study.

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this clinic. Other options are available; these include PCSK9 Inhibitors.

Your study doctor will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor. You can discuss if you want to have any treatment or if you want to choose another treatment such as other investigational drugs or medications to treat your condition.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive benefit from taking part in this study. Studies are a way for doctors to see if a drug is useful in treating a condition. Taking part in this research study may not help you or your hyperlipidaemia or ASCVD but will help AstraZeneca Pty Limited to answer the research questions.

Your taking part in this study may help scientists, doctors understand more about the treatment of hyperlipidaemia and ASCVD. By taking part in this study, your health will be monitored closely at study visits.

The information the study Sponsor, AstraZeneca Pty Limited receives from this study may help to better treat patients who have hyperlipidaemia or ASCVD.

9 What are the possible risks and disadvantages of taking part?

There is a risk that your hyperlipidaemia will not get better, or even get worse during the study. There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get.

Medical treatments often cause side effects. You may have none, some or all of the effects identified for the drug., and they may be mild, moderate or severe. All possible side effects of the drug are not known at this time. If you have any of the side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious or long lasting. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

Risks of AZD0780

AZD0780 has been studied in about 490 healthy volunteers and people with hyperlipidaemia. Animal studies have been done with AZD0780 to try and predict what type of side effects might occur in people. However, animal studies do not always predict human responses to medications.

From the results of these animal and laboratory studies, the following potential risks for AZD0780 have been identified:

- Vomiting
- Increased blood pressure.
- Changes in heart rhythm
- Dyspnoea (shortness of breath)
- Effects on Female Reproduction
- Possible Interference of AZD0780 with other drugs

Data from human studies for these risks are as follows:

- In a study in healthy participants 2 out of 45 participants experienced nausea and 1 participant out of 45 had vomiting. No participants on placebo had these symptoms. In a larger study where participants took a 30 mg dose of AZD0780, 4 out of 340 participants experienced nausea and 3 participants out of 340 experienced vomiting.
- In a small study in participants with high lipid levels, 1 out of 45 participants taking AZD0780 had high blood pressure while no participants taking the placebo had high blood pressure. In a larger study, 11 out of 340 participants had high blood pressure while 5 out of 86 participants taking placebo had high blood pressure
- QT Prolongation is an abnormal electrical activity in the heart or irregular heartbeat, which potentially could cause fainting or sudden death. During a study in which healthy participants took a few doses of AZD0780, one participant had an event of QT prolongation but also had other factors like a very fast heartbeat and anxiety that may have caused this finding. In a larger study of AZD0780 participant with high lipid levels no patients had this type of event reported.
- There has been no event of shortness of breath in any of the human studies conducted so far.

AZD0780 has been well tolerated in human studies without any major adverse events or side effects being observed.

Unknown risks

Because AZD0780 has limited exposure in humans, there is always a risk of some unexpected serious, life-threatening side effects occurring following the administration of a new experimental treatment. It is unknown whether some unexpected serious or life-threatening side effect could occur with AZD0780. You will be monitored closely for them and treated if they occur.

You could have an unwanted reaction when AZD0780 is taken with another medication.

Allergic reactions and anaphylaxis

Allergic reaction is always possible with a drug especially if you have not taken it before. Serious allergic reactions (anaphylaxis) that can be life-threatening may occur. Some things that happen during an allergic reaction to any type of medication are:

- Rash
- Joint pain
- Having a hard time breathing
- Wheezing when you breathe
- Sudden drop in blood pressure
- Swelling around the mouth, throat, or eyes
- Fast pulse
- Sweating

If you experience these symptoms, you should seek urgent medical help at an Emergency Department or call an ambulance.

Reproductive Risks

There is a risk of harm to an unborn baby if you become pregnant during this study.). Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and childbearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project.

Female participants of childbearing potential must use at least one form of an established highly effective contraception from the study start (screening visit) and for a period of 10 days after you have stopped taking the study treatment.

Female participants must use reliable birth control methods, such as birth control pills, patches, injections, or implants, or devices placed inside the uterus referred to as intrauterine devices (IUDs), intrauterine hormone-releasing systems, or permanent solutions involving surgery such as having your tubes tied or a partner who has had a surgery like vasectomy to prevent him from being able to make a female pregnant.

Not having sexual intercourse at all is an acceptable method, if that is your usual lifestyle. During the study, you will also need to take monthly urine pregnancy tests. Periodic abstinence (like counting days to track menstrual cycle to avoid sexual intercourse), withdrawal (male partner pulling out before ejaculation), use of chemicals to kill sperms, and relying on breastfeeding as a method of birth control are not acceptable as methods of birth control for this study. You should discuss methods of highly effective contraception with your study doctor.

If you become pregnant, you must stop taking the study drug and tell the study doctor immediately. You will be asked under a separate consent to provide information about you and your baby's health.

Risks associated with Study Tests and Procedures

Some of the study procedures may have possible side effects, risks and discomforts. You may experience none, some, or all. During the study you will have to have blood taken and have an ECG assessment. These are standard and routine procedures, and your Study Doctor will be able to explain these to you in detail and provide you with any risks and/or side effects associated with these.

Risks associates with taking blood samples:

Taking blood may cause discomfort at the site of the blood test, possible bruising, redness, and swelling around the site, bleeding at the site, feeling of light-headedness when the blood is taken, and rarely, an infection at the site of the blood test or fainting.

ECG (electrocardiogram):
The skin where the sticky pads are placed may become slightly red or may sting for a moment when they are removed.

10 What will happen to my test samples?

Your test samples will be analysed for the purposes of this research study and as outlined in this participant information sheet.

Your stored samples and the information collected about you during the study will be used by AstraZeneca, or its research partners to help answer study questions about the drug or hyperlipidaemia or ASCVD. Research partners are any organisation which collaborates with

the sponsor within the drug development programme. Your samples will be assigned a unique identifying code, but not your name or other individually identifiable information.

Some of your test samples taken during the study will be frozen and stored. These samples will be destroyed as soon as possible after the study tests for the drug development program are completed, unless you authorise the sponsor to use them for future research (see more information below).

Samples of your test samples obtained for the purpose of this research project will be transferred to the following central laboratory:

Labcorp located in Singapore

You may request that your stored samples be destroyed at any time by writing to the study doctor at the address listed in this form.

Optional Future Exploratory Biomarker Analysis

In addition to taking part in this clinical study, we would like to know if you agree to have an additional plasma and urine sample to be collected and used in future research projects with appropriate ethical approval.

Future research is important to advance science and public health but currently we cannot predict all details of future scientific research projects. These future scientific research projects are beyond the scope of this clinical research project including the use of your samples and data. These future studies may occur whilst the research project is ongoing or after the research project has finished.

If you consent to your coded data and test samples being used for future research, they will only be used for scientific health-related research to find new ways to detect, treat, prevent or cure health problems, or to develop new technologies and approaches that will assist with this activity, including developing machine learning and artificial intelligence technologies. These activities will not affect your care or any other decision affecting your life such as insurance rates or employment opportunities.

Your coded data and test samples may also be used jointly with information from other sources outside typical research project settings, e.g. from public research databases. However, they will not be combined with other information in a way that could identify you. Your coded data and test samples may also be anonymized for some of the future scientific research. If you agree to take part in future research, some of your coded data may be placed into one or more scientific databases.

Your coded data and test samples may also be shared with service providers or third parties including IT providers for the purposes of developing new technologies, system development and technical support.

AstraZeneca may generate and share internally or with other researchers an anonymised set of your data collected in the study (e.g., on www.clinicalstudydatarequest.com). This means your coded data will be stripped of your Patient code as well as of any other information that could reasonably be used to identify you such as your date of birth.

Some of the above-mentioned databases and research may be located outside Australia. The data protection and privacy laws which apply in those countries may not be as stringent as the laws in Australia / New Zealand. Appropriate safeguards and security measures will be taken in

order to protect and maintain the privacy and confidentiality of your personal information including your test samples and coded data.

Some research projects may require the analysis of your genetic information.

If you consent to the optional future research, we will collect an additional plasma sample and a urine sample taken at the randomisation visit and again at the End of Treatment Visit 10. Your additional test samples will be coded like the ones collected for the main clinical study.

All test samples will be securely stored on behalf of the sponsor at a secure laboratory facility located at Fisher Biosciences, 1 Woodside, Bishops Stortford, Hertfordshire, United Kingdom for a maximum of 15 years and will then be destroyed. Please note that the location of the test samples may change at the request of the sponsor.

Any additional data generated from your test samples will be stored as long as necessary for scientific research objectives and allowed by law and will be destroyed or fully deidentified (all codes and identifiers removed) thereafter. For more information on Sponsors internal Document Retention policy, you may go to www.astrazenecapersonaldataretention.com.

Your participation in future research is voluntary. You are entitled to withdraw your consent for future research at any time if you wish to withdraw, please inform your study doctor.

You may still continue to participate in the research project even if you choose to withdraw from the optional future research.

If you withdraw from the optional future research, your test samples will not be used for future research and your samples will be destroyed as soon as possible unless they have already been analysed.

Your coded data (either copied from the research project database or newly generated) will also be destroyed unless this information is already included in analyses or used in scientific publications. Once your coded data has been made anonymous we will be unable to destroy your test samples as we cannot identify these as your samples.

We may need to collect study coded data and test samples from many people over many years before we can know if the results of future research are meaningful.

Therefore, you will not receive individual results from future research projects. We will not give any such data to your doctor and we will not put them in your medical record as they are not individual valid results.

11 What if new information arises during this research project?

You will be made aware of any new findings that become available during the course of the study that may affect your willingness to take part in the study.

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it as soon as possible and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

12 Can I have other treatments during this research project?

Whilst you are participating in this research project, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

13 What if I withdraw from this research project?

Your participation in the study is voluntary which means you can stop your participation at any time. Leaving will not affect your care. If you want to stop taking the study drug, want to have a modified visit schedule or if you want to stop your participation, you should tell the study doctor. This notice will allow the study staff to discuss any health risks or special requirements linked to withdrawing.

The study doctor will then invite you to have an end of treatment visit (early-stop visit) to check your wellbeing. If you don't show up at a planned visit, the study doctor will try to reach you. If the study doctor cannot reach you, a variety of sources may be consulted to verify your wellbeing. This may include contacting individuals whose details you provided, your general physician, or searching publicly available sources, such as registries or other public databases. This is important for study results. It is not mandatory but would be helpful for the study if you explain to your study doctor why you wish to stop your study participation, in particular if you have experienced discomforts.

If you stop participating in the study, be aware, that this is a "study discontinuation", and not a withdrawal of or objection to consent for processing personal data, the study doctor will stop the collection of your data but your previously collected data and test samples will be kept and used to form part of the study results and comply with regulatory requirements, as allowed by law.

If you would like your data or test samples not to be used after you stop the study, you must inform the study doctor. In such case, your remaining test samples will be destroyed as soon as possible, but your coded data previously collected will be kept as required by clinical regulations.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects
- The drug/treatment/device being shown not to be effective
- The drug/treatment/device being shown to work and not need further testing
- Decisions made in the commercial interests of the sponsor or by local regulatory/ Health authorities, such as the Human Research Ethics Committee or the TGA (Therapeutic Good Administration, Australia).

Your study doctor may decide for your medical safety to stop your study drug or take you off the study. You may be taken off the study if your study doctor learns you did not give a correct medical history or did not follow instructions for the study. If you are taken off the study, you will no longer receive the study drug. If your study drug is stopped, your study doctor will closely monitor your overall health.

15 What happens when the research project ends?

How can I find out more about this study?

Trial Result Summaries are a short and easy to understand summary of the results of this study. These will be added to www.trialsummaries.com within Clinical Trial Transparency Global Standard should be consulted to determine timelines to be used to communicate lay language summary results 1 year of the last study participant's last site visit. You can visit www.trialsummaries.com website anytime to sign up to be notified via email when the trial results summary of your study is available. Or, please let your study doctor know if you need a printed copy of the document.

A description of this clinical trial will be available on http://www.clinicaltrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Technical Information about this research study and the results will be posted on:

- http://astrazenecaclinicaltrials.com/
- http://euclinicaltrials.eu
- https://www.clinicaltrialsregister.eu/

These websites will not contain any information about you.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

By signing this form, you consent to the Study Doctor and relevant research staff collecting, using, and sharing your personal and health information about you for the Study ("Personal Information") in accordance with the Australian *Privacy Act 1988* (Cth) and / or other applicable laws. Personal Information collected for this research project will include: your date of birth, your sex, your ethnic origin, your health and medical conditions and may also include genetic material. When you provide your consent, you are also agreeing to the possibility of your Personal Information being transferred to organisations outside of Australia.

Your consent to the use and sharing of your Personal Information does not have a specific end date, but you may withdraw your consent at any time by notifying the Study Doctor. Any information collected up until this point will be kept.

Who can access my medical records?

Your name, contact details, medical records and personal information as described above will be available to the Study Doctor and the team at the Life Clinical Research conducting the research project. Personnel acting on behalf of the sponsor, the ethics committee who approved this research, and regulatory authorities will also have access to this information as required by the study and do so by a duty of confidentiality. They will access your Personal Information to verify that the research project is being properly conducted.

This may include accessing your medical records remotely via a secure virtual connection if appropriate.

Who can access my coded data?

While the above-mentioned parties may have access to your medical records, your personal information will only be collected from your medical records and entered into study systems or databases after they have been coded. Your coded data will only be disclosed with your permission, except as required by law.

What is my data needed for?

When or if published this information will not identify you or be capable of identifying you.

The Sponsor may share your coded data with its research partners and others involved in the study testing and analysis for the purposes of the drug development programme. Your coded data and test samples may also be shared with scientific journals, so the study results can be reviewed by independent scientists and to ensure the accuracy of results.

Some of the research collaborators and others may be located outside Australia. If this other country does not have personal data protection standards equivalent to Australia, appropriate safeguards (such as contracts and technical security measures) will be adopted to protect and maintain the confidentiality of your data and test samples.

If another organisation takes over development or commercialisation of the study drug, your coded data or test samples may be transmitted to them. They will then have to protect your data and test samples in the same way as described in this Participant Information Sheet.

How long will my coded data and test samples be kept?

The study site and the sponsor are obliged to keep all study data for up to 25 years after the end of the study, unless there is a legal requirement for keeping them longer. Your coded data will then be deleted or made anonymous so that you cannot be identified.

Your exploratory and unused samples will also be destroyed, as soon as possible after the tests listed in section 3 for the drug development program are completed unless you agree for the sponsor to use them for future research.

How can I access my information?

In accordance with the Australian *Privacy Act 1988* (Cth) and other applicable laws, you have the right to request access to your personal information collected and stored for the purposes of the Study. You also have the right to request that any information with which you disagree be corrected. Please contact one of the researchers named at the end of this document if you would like to access your information.

17 Complaints and compensation

If you become ill or are injured while you are in this research study, you must tell your study doctor straight away.

There are two avenues that may be available to you for seeking compensation if you suffer an injury as a result of your participation in this research project:

- The pharmaceutical industry has set up a compensation process, with which the Sponsor AstraZeneca Pty Ltd, of this research project has agreed to comply. Details of the process and conditions are set out in the *Medicines Australia Guidelines for Compensation for Injury Resulting from Participation in a Company-Sponsored Clinical Trial*. In accordance with these Guidelines, the sponsor will determine whether to pay compensation to you, and, if so, how much. A copy of the Guidelines is available to you from the research staff on request.
- You may be able to seek compensation through the courts.

18 Who is organising and funding the research?

This research project is being conducted by AstraZeneca and sponsored in Australia by AstraZeneca Pty Ltd who are providing financial support to cover the costs of this research study. No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of Monash Health.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research 2023 (including all updates)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If there is an emergency, call 000 right away or go to your nearest emergency room and contact your study doctor as soon as you can.

Clinical Care contact person

Name	Dr. Andrew McCann
Position	Medical Director – Life Clinical Research
Telephone	07 3449 0036
Email	Andrew@LCR.Health

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	Paul Christensen
Position	Clinical Operations Director – Life Clinical Research
Telephone	0417 108 585
Email	Paul@LCR.Health

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	Monash Health Human Research Ethics Committee
HREC Executive Officer	HREC Executive Office
Telephone	(03) 9594 4611
Email	research@monashhealth.org

CONSENT FORM

Adult providing own consent

Title	A Phase III Study to Assess the Effect of AZD0780 on Low Density Lipoprotien Cholesterol in Patients with Clinical Atherosclerotic Cardiovascular Disease or are at Risk for a First Atherosclerotic Cardiovascular Disease Event
Short Title	AZURE-LDL
Protocol Number	D7960C00012
Project Sponsor	AstraZeneca Pty Ltd
Principal Investigator	Dr. Andrew McCann
Study site	Life Clinical Research

Declaration by Participant

I confirm that:

- The study doctor or study personnel assigned by the study doctor have explained the study to me comprehensively.
- I have had the opportunity to discuss the study with the study doctor and all my questions were answered.
- I have had an adequate amount of time to consider the study.
- I have read and understood all the above information related to the study or have had read to me in a language that I understand.
- I understand that I will receive a copy of this Participant Information and Consent Form once I have signed it.
- I understand that my decision to take part in the study is entirely voluntary. If I decide not to participate in the study or to stop my participation during the study, this will not affect my standard medical care.
- I have truthfully answered all questions about my medical history and will follow all rules listed in the document.
- I give permission for my doctors, other health professionals, hospitals, clinics or laboratories outside this clinic to release information to Life Clinical Research concerning my condition and treatment for the purposes of this project. I understand that such information will remain confidential.

I consent to take part in the research project and study procedures described herein. I understand that my participation also entails:

- My name, contact details and medical records collected during the study as described to me, to be accessed and reviewed by listed authorised people;
- My coded data being used by the sponsor or by people or companies acting on its behalf or working with the sponsor;
- My coded data being used by persons or organisations located in countries that do not have privacy laws or data protection rules equivalent to Australia. I understand that the sponsor monitors these uses and takes all possible measures to protect my privacy;
- My test samples being collected, shared and analysed as described herein and that this includes genetic analyses].

I further understand that I can make a choice about the topics listed below and that by ticking "Yes" I do give consent and that by ticking "No" I do not give consent:

OPTIONAL Exploratory Biomarker Analysis	Yes	No
My participation to optional tests/procedures: - Optional plasma sample for future biomarker analyses - Optional urine sample for future biomarker analyses	☐	☐

Name of Participant (please print) _____

Signature _____ Date _____

For patients unable to read the information and consent form.

Name of Witness* to the informed consent process (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. Witness must be 18 years or older. A legally accepted representative may be a witness.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/ Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.